

WHAT IS CLAIMED IS:

1. A method of treating a mammal having a disorder of cholesterol metabolism comprising administering to said mammal a therapeutically effective
5 amount of a compound that modulates the biological activity of ABCA1 polypeptide.

2. The method of claim 1, wherein said biological activity is *in vitro* lipid transport across a membrane.

10

3. The method of claim 2, wherein said lipid is a member selected from the group consisting of phospholipid and cholesterol.

4. The method of claim 2, wherein said ABCA1 polypeptide comprises the
15 amino acid sequence of SEQ ID NO: 1.

5. The method of claim 2, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

20 6. The method of claim 1, wherein said biological activity is *in vitro* ion transport across a membrane.

7. The method of claim 6, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

25

8. The method of claim 6, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

9. The method of claim 1, wherein said biological activity is *in vitro*
30 interleukin-1 transport across a membrane.

10. The method of claim 9, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

11. The method of claim 9, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

12. The method of claim 1, wherein said biological activity is *in vitro* ATP-hydrolysis.

13. The method of claim 12, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

14. The method of claim 12, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

15. The method of claim 1, wherein said biological activity is *in vitro* ATP-binding.

16. The method of claim 15, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

17. The method of claim 15, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

18. The method of claim 1 wherein said mammal is a mouse.

19. The method of claim 1 wherein said mammal is a human.

20. The method of claim 1, wherein said mammal has low HDL cholesterol levels relative to normal.

21. The method of claim 20 wherein said mammal is a mouse.

22. The method of claim 20 wherein said mammal is a human.

5 23. The method of claim 1 wherein said modulation is an increase in biological activity.

24. A method of treating a mammal having or at risk of developing a cardiovascular disease, comprising administering to said mammal a
10 therapeutically effective amount of a compound that modulates the biological activity of ABCA1 polypeptide.

25. The method of claim 24, wherein said biological activity is *in vitro* lipid transport across a membrane.

15

26. The method of claim 25, wherein said lipid is a member selected from the group consisting of phospholipid and cholesterol.

27. The method of claim 25, wherein said ABCA1 polypeptide comprises
20 the amino acid sequence of SEQ ID NO: 1.

28. The method of claim 25, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

25 29. The method of claim 24, wherein said biological activity is *in vitro* ion transport across a membrane.

30 30. The method of claim 29, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

30

31. The method of claim 29, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

32. The method of claim 24, wherein said biological activity is *in vitro* interleukin-1 transport across a membrane.

33. The method of claim 32, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

34. The method of claim 32, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

35. The method of claim 24, wherein said biological activity is *in vitro* ATP-hydrolysis.

36. The method of claim 35, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

37. The method of claim 35, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

38. The method of claim 24, wherein said biological activity is *in vitro* ATP-binding.

39. The method of claim 38, wherein said ABCA1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1.

40. The method of claim 38, wherein said ABCA1 polypeptide comprises amino acids 1-60 of SEQ ID NO: 1.

41. The method of claim 24 wherein said mammal is a mouse.

42. The method of claim 24 wherein said mammal is a human.

43. The method of claim 24, wherein said mammal has low HDL cholesterol levels relative to normal.

5

44. The method of claim 43 wherein said mammal is a mouse.

45. The method of claim 43 wherein said mammal is a human.

10

46. The method of claim 1 wherein said disease is selected from the group consisting of Alzheimer's disease, Niemann-Pick disease, Huntington's disease, x-linked adrenoleukodystrophy, and cancer.

47. The method of claim 46 wherein said mammal is a mouse.

15

48. The method of claim 46 wherein said mammal is a human.

49. The method of claim 24, wherein said cardiovascular disease is coronary artery disease, cerebrovascular disease, coronary restenosis, or peripheral vascular disease.

20

50. A method of preventing cardiovascular disease in a human, said method comprising administering to said human an expression vector comprising an *ABCA1* polynucleotide operably linked to a promoter, said *ABCA1* polynucleotide encoding an *ABCA1* polypeptide having *in vitro* *ABCA1* biological activity.

25

51. A method of preventing or ameliorating the effects of a disease-causing mutation in an *ABCA1* gene in a human, said method comprising introducing into said human an expression vector comprising a promoter

30

operably linked to an *ABCA1* polynucleotide encoding an *ABCA1* polypeptide having *in vitro* *ABCA1* biological activity.

52. A method of treating or preventing cardiovascular disease in an
5 animal, said method comprising administering to said animal a compound that mimics the activity of wild-type *ABCA1*.

53. The method of claim 52, wherein said animal is a human.

10 54. The method of claim 52 wherein said compound is a member selected from a group consisting of protein kinase A, protein kinase C, vanadate, okadaic acid, IBMX1, fibrates, γ -estradiol, arachidonic acid derivatives, WY-14,643, LTB₄, 8(s)HETE, thiozolidinedione antidiabetic drugs, 9-HODE, 13-HODE, nicotinic acid, HMG CoA reductase inhibitors, and compounds that increase PPAR-
15 mediated *ABCA1* expression.

55. The method of claim 52, wherein said cardiovascular disease is coronary artery disease, cerebrovascular disease, coronary restenosis, or peripheral vascular disease.

20

56. The method of claim 53 wherein said compound is a member selected from a group consisting of protein kinase A, protein kinase C, vanadate, okadaic acid, IBMX1, fibrates, γ -estradiol, arachidonic acid derivatives, WY-14,643, LTB₄, 8(s)HETE, thiozolidinedione antidiabetic drugs, 9-HODE, 13-HODE, nicotinic
25 acid, HMG CoA reductase inhibitors, and compounds that increase PPAR-mediated *ABCA1* expression.

30